METHODS FOR TREATING AND/OR COLLECTING INFORMATION REGARDING NEUROLOGICAL DISORDERS, INCLUDING LANGUAGE DISORDERS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] The present application relates to and claims priority to pending U.S. Provisional Application No. 60/432,073 (Attorney Docket No. 33734.8040US00), entitled "System and Method for Treating Parkinson's Disease and Other Movement Disorders," filed December 9, 2002, and pending U.S. Provisional Application No. 60/515,309 (Attorney Docket No. 33734.8055US), entitled "Methods for Treating and/or Collecting Information Regarding Neurological Disorders, Including Language Disorders," filed October 28, 2003, both incorporated herein by reference. The present application also relates to pending U.S. Application No. 10/072,700, filed February 7, 2002, and incorporated herein by reference.

TECHNICAL FIELD

[0002] The present invention is directed toward methods for treating and/or collecting information regarding neurological disorders, including language disorders, for example, aphasias.

BACKGROUND

[0003] A wide variety of mental and physical processes are controlled or influenced by neural activity in particular regions of the brain. For example, various physical or cognitive functions are directed or affected by neural activity within the various regions of the cerebral cortex. For most individuals, particular areas of the brain appear to have distinct functions. In the majority of people, for example, the areas of the occipital lobes relate to vision; the regions of the left inferior frontal lobes relate to language; portions of the cerebral cortex appear to

be involved with conscious awareness, memory, and intellect; and particular regions of the cerebral cortex as well as the basal ganglia, the thalamus, and the motor cortex cooperatively interact to facilitate motor function control.

[0004] Aphasias are neurological disorders that affect the language centers of the brain. Aphasias are typically caused by brain lesions that result from a stroke or head injury. Different aphasias result from damage to different portions of the brain's language centers. For example, Broca's aphasia typically results from a large frontal lobe lesion and causes the patient to speak with great effort in a nonfluent manner, while generally not affecting the patient's comprehension of single words and simple sentences. Wernicke's aphasia typically results from damage to the left temporal lobe of the brain and impacts the patient's comprehension of words and sentences, usually without affecting the patient's fluency. Global aphasia can affect both Broca's area and Wernicke's area of the brain and can accordingly adversely affect both the patient's comprehension and speech fluency. Conduction aphasia is caused by damage to structures that interact with the major language areas of the brain. Conduction aphasia does not have as substantial an effect on the patient's comprehension or fluency as do other aphasias, but reduces the patient's ability to repeat sentences verbatim or easily name pictures and objects.

[0005] Practitioners have developed imaging techniques to isolate the portions of the brain affected by various aphasias. For example, Perani, et al. disclose identifying and tracking neurological functioning connected with language-based activities by obtaining functional magnetic resonance imaging (fMRI) data while the patient executes language-based tasks (see "A fMRI Study of Word Retrieval in Aphasia," Brain and Language 85 (2003) pp. 357-368). Practitioners have also treated aphasia, for example, with conventional and/or melodic speech therapies, with drugs (e.g., amphetamines and other neuro-stimulatory agents) and with transcutaneous magnetic stimulation (TMS) applied to the brain. However, these techniques all suffer from drawbacks. In particular, the efficacies of speech therapy and drug-based techniques have not been conclusively demonstrated, and the effects of TMS are short-lived.

BRIEF DESCRIPTION OF THE DRAWINGS

[0006] Figure 1A is a flow chart illustrating a method for treating a language disorder in accordance with an embodiment of the invention.

[0007] Figure 1B is a flow chart illustrating details of a method for selecting a stimulation site used for treating language disorders in accordance with another embodiment of the invention.

[0008] Figure 2 is a partially schematic, isometric illustration of a human brain illustrating areas associated with language comprehension and production and suitable for stimulation in accordance with embodiments of the invention.

[0009] Figure 3 is a partially schematic generally horizontal section through a human brain illustrating reference features suitable for locating stimulation sites in accordance with other embodiments of the invention.

[0010] Figure 4 is a partially schematic, isometric illustration of a human brain having an electrode assembly positioned for stimulation in accordance with an embodiment of the invention.

[0011] Figure 5 is a partially schematic, isometric illustration of a human brain and an electrode assembly configured in accordance with another embodiment of the invention.

[0012] Figure 6 is a partially schematic, side view of a patient's upper body, head and neck, along with an electrode assembly positioned in accordance with yet another embodiment of the invention.

[0013] Figure 7 is a cross-sectional illustration of an electrode system positioned in a patient's skull in accordance with an embodiment of the invention.

[0014] Figure 8 is a partially schematic cross-sectional side view of an electrode system positioned in a patient's skull and having an electrode urged against a portion of the patient's brain in accordance with another embodiment of the invention.

[0015] Figure 9 is a partially schematic, side elevational view of an electrode system positioned in the patient's skull in accordance with still another embodiment of the invention.

[0016] Figure 10 is a flow chart illustrating a method for collecting information while stimulating a patient's brain in accordance with another embodiment of the invention.

DETAILED DESCRIPTION

[0017] The following disclosure describes several methods for collecting information regarding neurological disorders, including language disorders, and methods for treating such disorders using electrical stimulation, for example, cortical stimulation. Cortical stimulation has been applied in other contexts, for example to enhance the recovery of cortical functions after a brain injury affecting motor capabilities. Several features of methods in accordance with embodiments of the invention are set forth and described in Figures 1A-10. It will be appreciated that methods in accordance with other embodiments of the invention can include additional procedures or features different than those shown in Figures 1A-10. Additionally, methods in accordance with several embodiments of the invention may not include all of the features shown in these Figures.

[0018] Figure 1A is a flow chart illustrating a method 100 for treating language disorders in accordance with an embodiment of the invention. In one aspect of this embodiment, the method 100 includes selecting a brain stimulation site located within the patient's skull (method portion 102). At least one electrode can then be positioned at the stimulation site (method portion 104). The method 100 can further include coupling the electrode(s) to a source of electrical potential (method portion 106) and at least reducing a language disorder of the patient by applying electrical stimulation directly to the stimulation site via the electrode(s) (method portion 108).

[0019] In one particular aspect of this embodiment, the patient's language disorder can be entirely eliminated. In another particular aspect of this embodiment, the effects of the disorder can at least be diminished. In a further aspect of either embodiment, the stimulation site can be selected to be on the left side of the patient's brain, e.g., at or proximate to the language centers of the brain. In another aspect of these embodiments, the homologous structures on the right side

of the patient's brain can be stimulated in addition to or in lieu of stimulating the left side of the patient's brain. Further details of the areas of the brain selected for stimulation, and the devices that apply the stimulation are discussed later with reference to Figures 2-10.

[0020] Referring next to Figure 1B, the process of selecting a stimulation site (process portion 102) can include directing the patient to perform a language-based task (process portion 110). The method can further include directing information to be collected while the patient performs the language-based task, with the information corresponding to a level of neural activity in the patient's brain while the task is performed (process portion 112). In one embodiment, the foregoing process portions can be completed while the patient is under the influence of an amphetamine or other neuroexcitatory drug, and in other embodiments, such agents are not present in the patient's body during the procedure.

[0021] In one embodiment, process portion 112 can be carried out at least in part by a human operator, for example, a technician or physician who operates an imaging system. In another embodiment, the process of directing the collection of information can be performed partially or entirely by a computer, for example, by a hardware- and/or software-based routine that collects the information corresponding to the level of neural activity. In either embodiment, the information can take several forms and/or can correspond to the level of neural activity in the patient's brain by virtue of any of several techniques, as described below. As is also described below, a practitioner can direct the patient to perform one or more of a variety of language-based tasks that generate a neural response corresponding to the collected information.

[0022] In a particular aspect of an embodiment of the invention, the language-based task performed by the patient does not require the patient to actually vocalize. Instead, the patient can be directed to merely think of a word, letter, phrase or other language component. For example, the patient can be directed to silently generate a verb associated with a common noun, silently repeat a noun, silently retrieve a word based on a letter cue, or silently retrieve a word based on a

visual cue. In particular cases, the patient can be directed to think of words beginning with the letter "C," for example, or can be shown a picture of a cat and asked to think of the word represented by the picture. The patient can also be asked to respond nonverbally to an oral task that requires the patient to understand the difference between two auditory commands. In any of these embodiments, the patient need not use motor neurons to execute the selected task. An advantage of this arrangement is that reducing the number of motor neurons active while the patient performs the selected task can more clearly highlight those areas of the brain associated purely with the cognitive aspect of the language-based task. Put another way, this technique can reduce or eliminate the recorded activity of motor neurons, which might otherwise clutter or obscure the cognitive, language-based information of interest.

[0023] In other embodiments, the patient can be directed to perform any of the above tasks verbally. The practitioner can direct the patient to perform a verbal task when, for example, the motor activity associated with speech production will clearly not obscure neural responses associated with non-motor aspects of language-based tasks, and/or when it is desirable to locate and/or stimulate regions of the brain associated with motor aspects of the language-based tasks. In still further embodiments, the patient can be directed to perform a variety of language-based tasks and the information collected while the patient performs each task can be combined to aid the practitioner in determining a stimulation site. This technique can be used to identify multiple stimulation sites and/or to more definitively or precisely locate a particular stimulation site. In any of these embodiments, the methods described above include collecting information, such as imaging information, while the patient performs the task, as described in greater detail below.

[0024] The collected information can take the form of an image, generated using functional magnetic resonance imaging (fMRI) techniques, magnetic resonance imaging (MRI) techniques, computed tomography (CT) techniques, single photon emission computed tomography (SPECT) techniques, positron emission tomography (PET) techniques and/or other techniques. In any of these

embodiments, a practitioner can view the image and, based at least in part on the image, identify a stimulation site for treating the language disorder. For example, the images can be color-coded or can have other distinguishing characteristics that allow the practitioner to distinguish active regions from inactive regions. In a particular embodiment, the active regions can be identified by a relatively elevated blood oxygen level, and in other embodiments, these regions can be identified on the basis of other characteristics.

[0025] In other embodiments, the foregoing techniques can be used to generate a digital representation of brain activity without necessarily generating a visible image. In a particular aspect of these embodiments, an algorithm or other computer-based method can be used to determine the stimulation site, based upon the digital representation described above. Whether or not the collected information is in the form of a visually accessible image, it can aid the practitioner in determining where to implant electrodes for applying electrical stimulation. The locations for the electrodes and the techniques for placing the electrodes at the stimulation sites are described in greater detail below with reference to Figures 2-9.

[0026] Methods in accordance with still further embodiments of the invention can include subsets of the method portions shown in Figure 1A-1B. For example, a method in accordance with one embodiment of the invention includes directing the patient to perform a language-based task and then directing information to be collected, with the information corresponding to a level of neural activity in the patient's brain while the patient performs the language-based task. The method can further include selecting a stimulation site based at least in part on the information. The stimulation site can be located within the patient's skull and can receive an electrode coupleable to an electrical current.

[0027] Figure 2 is an isometric, left side view of the brain 120 of a patient P. As described above, certain sectors of the brain 120 are typically responsible for language-based tasks. These sectors can be identified using the techniques described above, and can be selected as stimulation sites. Accordingly, the

sectors can be targeted to receive direct electrical stimulation for reducing and/or eliminating the effects of a language disorder.

[0028] In one embodiment, the targeted areas of the brain 120 can include Broca's area 124 and/or Wernicke's area 125. In other embodiments, sections of the brain 120 anterior to, posterior to, or between these areas can be targeted in addition to or in lieu of targeting Broca's area 124 and Wernicke's area 125. For example, the targeted areas can include the middle frontal gyrus 121, the inferior frontal gyrus 122 and/or the inferior frontal lobe 123 anterior to Broca's area 124. In other embodiments, the areas targeted for stimulation can include the superior temporal lobe 127, the superior temporal gyrus 128, and/or the association fibers of the arcuate fasciculcus 126. In still further embodiments, the targeted areas can include the inferior parietal lobe 129 and/or other structures, including the supramarginal gyrus, angular gyrus, retrosplenial cortex and/or the retrosplenial cuneus of the brain 120.

[0029] Figure 3 is a partially schematic, approximately horizontal section through the brain 120 described above with reference to Figure 2. The stimulation sites described above with reference to Figure 2 can be identified with reference to anatomical features of the patient, for example, the patient's nose. In other embodiments, the stimulation site can be identified with reference to fiducials 133 positioned in the patient's skull 132. Accordingly, the location of the fiducials 133 can appear on the image (or other display format) used to present the neural activity information and identify the corresponding stimulation sites.

[0030] Figure 4 is an isometric illustration of the brain 120 with an electrode assembly 140 positioned to provide stimulation in accordance with an embodiment to the invention. In one aspect of this embodiment, the electrode assembly 140 includes a support 141 carrying a plurality of electrodes 142 (eight are shown in Figure 4). In a further aspect of this embodiment, the electrode assembly 140 is positioned to cover a plurality of the areas (described above) responsible for carrying out language-based tasks. For example, in one embodiment, the electrode assembly 140 can be sized to extend generally from the inferior frontal lobe 123 to the inferior parietal lobe 129, and can include electrodes 142 located

to stimulate any of a plurality of areas between and adjacent to these structures. In any of these embodiments, the electrode assembly 140 can also include a lead 143 coupled to a power supply and/or a pulse system, as described in greater detail below with reference to Figure 6.

[0031] One feature of an embodiment of the electrode assembly 140 described above with reference to Figure 4 is that it can include an array of electrodes 142 that are spaced apart from each other, for example, along two transverse axes. Accordingly, each electrode 142 can be positioned to stimulate a particular region of the brain 120. An advantage of this arrangement is that a practitioner can stimulate multiple sites of the brain 120 (either simultaneously or sequentially) with a single electrode assembly 140. In one embodiment, the practitioner can stimulate multiple sites of the brain 120 (rather than a single site) to produce enhanced benefits for the patient. In another embodiment, the practitioner can use an electrode assembly 140 having an array of electrodes 142 when it is initially uncertain which area(s) of the patient's brain 120 should be stimulated to produce the most beneficial effect. Accordingly, a practitioner can stimulate a particular area of the brain 120 with one of the electrodes 142, observe the effect on the patient, and if the effect is not the desired effect, stimulate another area of the brain 120 with another of the electrodes 142 and observe the resulting effect, all with a single, implanted assembly 140. In still another embodiment, the practitioner can apply stimulation to different sites for different lengths of time, and/or the practitioner can independently vary other stimulation parameters applied to the electrodes 142. In any of these embodiments, the signal applied to the electrodes 142 can be varied randomly or pseudo-randomly. Further details of the signals applied to the electrodes 142 are described below with reference to Figure 6.

[0032] In another embodiment shown in Figure 5, the practitioner can implant a generally strip-shaped electrode assembly 540 in the patient P. In one aspect of this embodiment, the electrode assembly 540 can include an elongated support 541 carrying a plurality of linearly aligned electrodes 542 coupled to a lead 543. The electrode assembly 540 can be positioned to extend over a relatively narrow

band between the inferior frontal lobe 123 and the inferior parietal lobe 129. In one aspect of this embodiment, the electrode assembly 540 can include six electrodes 542, and in other embodiments, the electrode assembly 540 can include more or fewer electrodes 542. In any of these embodiments, the electrodes 542 can be selectively activated, simultaneously or sequentially, in a manner generally similar to that describe above to provide the patient with a therapeutically effective treatment.

[0033] In other embodiments, the electrode assembly can have arrangements other than those described above. For example, other electrode assemblies can have support members with shapes other than those shown in Figures 4 and 5, including irregular shapes. In still further embodiments, the electrodes can be distributed over the support members or irregular patterns, for example, to align with sites at the brain 120 most likely to be selected for stimulation.

[0034] In one aspect of embodiments described above with reference to Figures 4 and 5, the electrode assemblies are positioned over the left hemisphere of the patient's brain because the language centers of the brain are typically concentrated there. In other embodiments, the electrode assemblies can be positioned on the right side of the patient's brain to stimulate right hemisphere neurons. For example, as shown in Figure 6, an electrode assembly 540 generally similar to that described above with reference to Figure 5 can be positioned over the right side of the patient's brain 120 between the inferior frontal lobe 123 and the inferior parietal lobe 129. Accordingly, the electrode assembly 540 can be positioned adjacent to the brain structures homologous to those described above with reference to Figures 2-4.

[0035] In one aspect of this embodiment, the stimulation applied to the right side of the patient's brain 120 can recruit right-side neurons to take over functions normally provided by (now defective) tissue on the left side of the patient's brain 120. In another embodiment, (used, for example, when it is determined that recruiting homologous right-side neurons is actually detrimental to the patient's recovery of language-based functionality), the stimulation is applied to the right side of the patient's brain to impede or inhibit the body's attempts to recruit right-

side neurons. In a particular aspect of this embodiment, the manner in which this stimulation is applied (e.g., the level of the voltage or current applied and/or the manner in which the voltage or current is varied or modulated) can determine whether the effect of the right-side neurons is enhanced or inhibited. In another embodiment, the location of the electrodes can determine whether the effect of the right-side neurons is enhanced or inhibited. In either embodiment, it can be advantageous to have a plurality of electrodes 542 (as shown in Figure 6) available on the right side of the brain to allow flexibility in treating the patient's language-based disorder. The plurality of electrodes 542 can be arranged along a single axis (as shown in Figure 6), or along multiple axes (e.g., as shown in Figure 4), or in an irregular pattern. In still another embodiment, the foregoing technique can be used to inhibit the body's attempts to recruit left-side neurons, for example, when it is determined that recruiting such neurons is actually detrimental to the patient's recovery.

[0036] In another aspect of an embodiment shown in Figure 6, the electrode assembly 540 can form a portion of a system 650 that also includes a pulse generator 651. For purposes of illustration, two alternative examples of pulse generators 651 are shown in Figure 6 as a first pulse generator 651a and a second pulse generator 651b. The first pulse generator 651a can be implanted at a subclavicular location in the patient P, and the second pulse generator 651b can be implanted above the neck, posteriorly to the ear of the patient P. Either pulse generator 651 can be coupled to the electrode assembly 540 with the lead 543 and can provide electrical signals that stimulate the adjacent neurons, as described in greater detail below.

[0037] In one embodiment, the electrical signals can be applied to a single one of the electrodes 542 to provide a monopolar pulse of current to a small area of the brain 120. Accordingly, the system 650 can include a return electrode, which can be a portion of a pulse generator 651, or a separate electrode implanted elsewhere in the patient P (e.g., on the other side of the patient's brain 120 or at a subclavicular location). In other embodiments, electrical current can be passed through all of the electrodes 542 or only a subset of the electrodes 542 to activate

larger or different populations of neurons. In one aspect of these embodiments, the potential applied to the electrodes 542 can be the same across all of the activated electrodes 542 to provide monopolar stimulation at the stimulation site. In other embodiments, some of the electrodes 542 can be biased with a positive polarity and other electrodes 542 can be biased with a negative polarity. This embodiment provides a bipolar stimulation to the brain 120. The particular configuration of the electrodes 542 activated during treatment can be optimized after implantation to provide the most efficacious therapy for the patient P.

[0038] The particular waveform of the applied stimulus depends upon the symptoms of the patient P. In one embodiment, the stimulus includes a series of biphasic, charge balanced pulses. In one aspect of this embodiment, each phase of the pulse is generally square. In another embodiment, the first phase can include a generally square wave portion representing an increase in current above a reference level, and a decrease below the reference level. The second phase can include a gradual rise back to the reference level. The first phase can have a pulse width ranging from about 25 microseconds to about 400 microseconds. In particular embodiments, the first phase can have a pulse width of 100 microseconds or 250 microseconds. The total pulse width can range up to 500 milliseconds.

[0039] The voltage of the stimulus can have a value of from about 0.25 V to about 10.0 V. In further particular embodiments, the voltage can have a value of from about 0.25 V to about 5.0 V, about 0.5 V to about 3.5 V, about 2.0 V to about 3.5 V or about 3 V. The voltage can be selected to be below a level that causes movement, speech or sensation in the patient (e.g., subthreshold) or above such a level (e.g., suprathreshold). In certain embodiments, the practitioner may control the current applied to the patient, in addition to or in lieu of controlling the voltage applied to the patient.

[0040] The frequency of the stimulus can have a value of from about 25 Hz to about 250 Hz. In particular embodiments, the frequency can have a value of from about 50 Hz to about 150 Hz, or about 100 Hz. The stimulation can be applied for a period of 0.5 hour - 4.0 hours, and in many applications the stimulation can be

applied for a period of approximately 0.5 hour – 2.0 hours, either during language-based therapy (e.g., language comprehension training) or before, during and/or after such therapy. In other embodiments, the stimulation can be applied continuously, or only during waking periods but not during sleeping periods. It may be particularly effective to treat language disorders by applying stimulation before, during, and/or after language-based therapy because the language centers of the brain may be active during many periods of time in addition to active therapy periods. In particular aspects of this embodiment, the characteristics (e.g., current, voltage, waveform, pulse duration, frequency) are different depending on whether the stimulation is applied before, during or after the language-based therapy. In still further embodiments, the stimulation can be applied while a selected drug (e.g., an amphetamine or other neuroexcitatory agent) is active. In other embodiments, such drugs are not administered. Examples of specific electrical stimulation protocols for use with an electrode array at an epidural stimulation site are as follows:

Example 1

An electrical stimulus having a current of from about 3 mA to about 10 mA, an impedance of 500 to 2000 Ohms, a pulse duration of 160 microseconds, and a frequency of approximately 100 Hz. The therapy is not applied continuously, but rather during 30 - 120 minute intervals, associated with language-based therapy.

Example 2

The stimulus has a current of from about 3 mA to about 6 mA, a pulse duration of approximately 150 - 180 microseconds, and a frequency of approximately 25 Hz - 31 Hz. The stimulus is applied continuously during waking periods, but it is discontinued during sleeping periods to conserve battery life of the implanted pulse generator.

Example 3

> The stimulus has a current of from about 3 mA to about 6 mA, a pulse duration of approximately 90 microseconds, and a frequency of approximately 30 Hz. This stimulus is applied continuously during waking and sleeping periods, but it can be selectively discontinued during sleeping periods.

[0041] In one aspect of embodiments of the systems described above with reference to Figures 4-6, an electrode assembly having multiple electrodes is positioned at the cortex of the brain 120. Further details of such placements are described below with reference to Figures 7-9. In other embodiments, portions of the electrode assemblies can extend into or beneath the cortex to stimulate interior portions of the brain 120, including deep brain tissue. In still further embodiments, the electrode assembly can include a single electrode or one or more electrode pairs, also described in greater detail below with reference to Figures 7-9.

[0042] Figure 7 is a cross-sectional view of a stimulation system 750 configured and implanted in accordance with an embodiment of the invention. In one aspect of this embodiment, the stimulation system includes a support member 741, an integrated pulse system 751 (shown schematically) carried by the support member 741, and first and second electrodes or contacts 742 (identified individually by reference numbers 742a and 742b). The first and second electrodes 742 are electrically coupled to the pulse system 751 and are carried by the support member 741.

[0043] The support member 741 can be configured to be implanted in the skull 132 or another region of a patient P above the neckline. In one embodiment, for example, the support member 741 includes a housing 744 and an attachment element 745 connected to the housing 741. The housing 744 can be a molded casing formed from a biocompatible material, and can have an interior cavity for carrying the pulse system 751 and a power supply. The housing 744 can alternatively be a biocompatible metal or another suitable material. The housing 744 can have a diameter of approximately 1-4 cm, and in many applications the

housing 744 can be 1.5-2.5 cm in diameter. The thickness T of the housing 744 can be approximately 0.5-4 cm, and can more generally be about 1-2 cm. The housing 744 can also have other shapes (e.g., rectilinear, oval, elliptical) and other surface dimensions. The stimulation system 750 can weigh 35g or less and/or can occupy a volume of 20cc or less. The attachment element 745 can include a flexible cover, a rigid plate, a contoured cap, or another suitable element for holding the support member 741 relative to the skull 132 or other body part of the patient P. In one embodiment, the attachment element 745 includes a mesh, e.g., a biocompatible polymeric mesh, metal mesh, or other suitable woven material. The attachment element 745 can alternatively be a flexible sheet of Mylar, polyester, or another suitable material.

[0044] In one aspect of an embodiment shown in Figure 7, the stimulation system 750 is implanted in the patient P by forming an opening in the scalp 734 and cutting a hole 735 completely through the skull 132. The hole 735 can also pass through the dura mater 736 for subdural applications (shown), or the hole 735 can pass through the skull 132 but not the dura mater 736 for epidural applications. The hole 735 can be sized to receive the housing 744 of the support member 741, and in most applications the hole 735 can be smaller than the attachment element 745. A practitioner can insert the support member 741 into the hole 735 and then secure the attachment element 745 to the skull 132. The attachment element 745 can be secured to the skull 132 using a plurality of fasteners 746 (e.g., screws, spikes, etc.) or an adhesive. In another embodiment, a plurality of downwardly depending spikes can be formed integrally with the attachment element 745 to provide anchors that can be driven into the skull 132.

[0045] The embodiment of the stimulation system 750 shown in Figure 7 is configured to be implanted in the patient P so that the electrodes 742 are juxtaposed to a desired cortical stimulation site. The housing 744 can project from the attachment element 745 by a distance D_1 such that the electrodes 742 are positioned at least proximate to the dura mater 736 or the pia mater 737 surrounding the cortex 738. The electrodes 742 can project from the housing 744 as shown in Figure 7. In the particular embodiment shown in Figure 7, the

electrodes 742 project from the housing 744 by a distance D_2 so that the electrodes 742 press against a desired surface of the brain 120. The distance D_2 is from 0.1 mm to about 5 cm in some embodiments, and has other values in other embodiments. In still further embodiments, the electrodes 742 are flush with the housing 744. The electrodes 742 can be separate conductive members attached to the housing 744, or the electrodes 742 can be integral surface regions of the housing 744.

[0046] The configuration of the stimulation system 750 is not limited to the embodiment shown in Figure 7. For example, in other embodiments, the housing 744, and the attachment element 745 can be configured to position the electrodes 742 in several different regions of the brain. In particular embodiments, the housing 744 and the attachment element 745 can be configured to position the electrodes 742 deep within the cortex 738 or against the dura mater 736.

[0047] The pulse system 751 shown in Figure 7 generates and/or transmits electrical pulses to the electrodes 742 to stimulate a cortical region of the brain 120. The particular embodiment of the pulse system 751 shown in Figure 7 is an "integrated" unit in that the pulse system 751 is carried by the support member 741. The pulse system 751, for example, can be positioned within the housing 744 so that the electrodes 742 can be carried by the housing 744 and connected directly to the pulse system 751 without having external leads outside the stimulation system 750. The distance between the electrodes 742 and the pulse system 751 can be less than 4 cm, for example, 0.10 to 2.0 cm. The stimulation system 750 can accordingly provide electrical pulses to the stimulation site without requiring a remote implanted pulse generator, which is connected to the electrodes 742 with surgically tunneled cables. In other embodiments, the pulse generator can be implanted separately from the electrodes, for example, in a manner generally similar to that described above with reference to Figure 6. In still further embodiments, signals can be transmitted to the electrodes 742 from a remote location outside the patient's body via a wireless (e.g., RF) link.

[0048] Figure 8 is a cross-sectional view of a stimulation system 850 configured and implanted in accordance with an embodiment of the invention. In one aspect

of this embodiment, the stimulation system 850 includes a driving element 860 coupled to the electrodes 742 to mechanically urge the electrodes 742 away from the housing 744. In another embodiment, the driving element 860 can be positioned between the housing 744 and the attachment element 745, and the electrodes 742 can be attached directly to the housing 744. The driving element 860 can include a compressible member, for example, an open or closed cell biocompatible compressible foam, or a compressible solid (e.g., silicon rubber). In other embodiments, the driving element 860 can include a fluid-filled bladder, a spring, or any other suitable element that resiliently and/or elastically exerts a force against the electrodes 742.

[0049] In one aspect of an embodiment shown in Figure 8, the driving element 860 is compressed slightly upon implantation so that the electrodes 742 contact the stimulation site. For example, the compressed driving element 860 can gently press the electrodes 742 against the surface of the pia mater 737. It is expected that the driving element 860 will provide a uniform, consistent contact between the electrodes 742 and the pial surface of the cortex 738. The stimulation system 850 is expected to be particularly useful when the implantable device is attached to the skull 132 and the stimulation site is on the pia mater 737 or the dura mater 736. It can be difficult to position the electrodes 742 against the pia mater 737 because the distance between the skull 132 and the dura mater 736 or the pia mater 737 varies as the brain 120 expands and contracts relative to the skull 132, and also because this distance varies from one patient P to another. The driving element 860 of the stimulation system 850 can compensate for the different distances between the skull 132 and the pia mater 737 so that a single type of device can better fit several different patients P. Moreover, the driving element 860 can change the position of the electrodes 742 as the brain 120 moves within the skull 132.

[0050] Figure 9 is a cross-sectional view of a stimulation system 950 configured and implanted in accordance with another embodiment of the invention. The stimulation system 950 can include a support member 941, an integrated pulse system 951 (shown schematically) carried by the support member 941, a driving

element 960 carried by the support member 941, and an electrode or contact 942a carried by the driving element 960. The contact 942a is electrically coupled to the pulse system 951 by a lead 943a. The driving element 960 can be a compliant material having a cavity 961 filled with a fluid such as saline or air. In another embodiment, the stimulation system 950 can further include an optional return electrode 942b carried on the opposite side of the support structure 941. The return electrode 942b can be electrically coupled to the pulse system 951 by a return lead 943b.

[0051] To implant the stimulation apparatus 960, a burr hole 935 is cut completely through the skull 132 of the patient P at a predetermined location identified according to the methods set forth above. The burr hole 935 can also pass through the dura mater (not shown Figure 9). After forming the burr hole 935, a ferrule 947 is placed in the burr hole 935, and a threaded barrel 948 is welded or otherwise attached to the ferrule 947. A position ring 949 is then threaded along the threads of the barrel 948 to a desired height. The stimulation system 950 is placed in the burr hole 935 until a rim 952 projecting from the support member 941 engages the position ring 949. A lock ring 953 is then threaded onto the barrel 949 until it engages the rim 952. The position ring 949 and the lock ring 953 hold the support member 941 at a desired height relative to the surface of the patient's brain 120.

[0052] In one aspect of the embodiments described above with reference to Figures 1A-9, information is collected on the activity of the brain prior to implanting any of the foregoing stimulation systems. Accordingly, the collected information can guide the practitioner as the practitioner determines where to apply the stimulation. In a method in accordance with another embodiment of the invention (shown in Figure 10), such information can be collected while the stimulation system is activated. For example, a method 1000 in accordance with an embodiment of the invention includes directing a patient to perform a task (process portion 1002), directing information to be collected corresponding to a level of neural activity in the patient's brain while the patient performs the task (process portion 1004), and applying an electrical stimulation to the patient's brain while

directing the information to be collected (process portion 1006). In one aspect of this embodiment, the task performed by the patient can be a language-based task, for example, any of the tasks described above with reference to Figures 1A-1B. In another embodiment, the task can be another type of task (for example, a motor task) which also generates a detectable response in the patient's brain. In any of these embodiments, the information can take the form of visually accessible images (e.g., using fMRI, MRI, CT, or PET techniques), or the information can take other forms that are not necessarily visually accessible.

[0053] The information collected while the stimulation system is active can be used to determine whether the stimulation system is creating the desired response in the patient's brain, and/or whether the response is occurring in the desired area of the patient's brain. This technique can be used to provide feedback on the efficacy of the stimulation system and can also be used to adjust aspects of the stimulation system. For example, when the stimulation system includes a plurality of electrodes, the foregoing technique can be used to determine which of the electrodes is providing the desired response. This technique can also be used to determine whether the voltage level (and/or the variation of the voltage level) of the signals applied to the electrodes produces the desired effect. Accordingly, such techniques can be used in addition to or in lieu of receiving direct feedback from the patient to determine the efficacy of the treatment. Such techniques can also be used to tailor the manner in which the treatment is administered.

[0054] From the foregoing, it will be appreciated that specific embodiments of the invention have been described herein for purposes of illustration, but that various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.